

REMARKS

Applicants wish to thank Examiner Johannsen for the courtesies extended to Applicant's representatives during the telephonic interview of January 3, 2008. The substance of that interview is reflected in the Interview Summary mailed by Examiner Johannsen on January 4, 2008, and the amendments and remarks contained herein.

Applicants also acknowledge and thank the Examiner for indicating, both in the Final Office Action and the telephonic interview, that claim 3, encompassing the amplification primers of SEQ ID NOs: 1-8, are allowable if rewritten in independent form.

Status of the Claims

This paper amends claims 1, 4, 8-10, 12, 30-31, 36, 39, and 43-45; cancels claims 2-3, 19-29, 33-35 and 37-38; and adds new claims 47-48. Accordingly, after amendment, claims 1, 4-18, 30-32, 36, 39-42, and 44-48 are pending and under examination, and claim 43 is pending but withdrawn. No new matter is added in these claim amendments.

Support for the claim amendments is found in the canceled claims and generally throughout the specification and in the Examples. Specifically, Examples 3.8.1.1 and 3.8.1.2 describe the construction of a multiplex primer mix for PCR amplification containing primers of SEQ ID NOs: 1-4 and 5-8, respectively. These amplification primer mixes are used in Examples 4.1-4.3. Furthermore, Examples 3.8.5 and 4.4 describe the construction and use, respectively, of an extension primer mix containing a plurality of primers for detecting a variety of CYP2D6 polymorphisms.

Objections to the Specification

The Examiner's objection to the amendments to the specification submitted on May 1, 2007, as containing several informalities is acknowledged, as is the Examiner's objection to the entry of the substitute specification submitted August 31, 2007. Applicant submits herewith a substitute specification (and corresponding marked-up copy showing all amendments thereto) in

which the informalities have been addressed. Pursuant to MPEP 608.01(q), the marked up text in the marked up copy submitted herewith reflects changes relative to the immediate prior version of the specification of record.

The substitute specification contains no new matter and its entry into the record is respectfully requested.

Rejections Under 35 U.S.C. §112, second paragraph

Multiple claims stand rejected for indefiniteness on several grounds. These rejections are rendered moot in view of the amended claims, and should be withdrawn.

Rejections Under 35 U.S.C. §102

Claims 1-2, 4, 6-9, 11-20, 22, 24-27, 29-32, and 46 stand rejected as anticipated by Anastasio et al. (WO 02/38589), as evidenced by Goelet et al. (WO 92/15712). The Examiner alleges that Anastasio et al. describes various cytochrome P450 2D6 (“CYP2D6”) polymorphisms and methods for genotyping and haplotyping the same. The Examiner acknowledges that Anastasio et al. does not specifically disclose Applicants’ claimed method for determining CYP2D6 genotype, but notes that Anastasio et al. instructs that the polymerase-mediated primer extension methods of Goelet et al. may be used. The Examiner alleges that the methods described in Goelet et al. meet all of the limitations of the rejected claims. Applicants respectfully traverse this rejection.

Claims 1 and 36 encompass methods for detecting the presence or absence of CYP2D6 polymorphisms (i.e., determining CYP2D6 genotype) by (i) amplifying a CYP2D6 gene sequence using multiplex amplification primers of SEQ ID NOs: 1-4 and 5-8, respectively, and (ii) performing a primer extension reaction using a plurality of extension primers that specifically bind to the CYP2D6 gene sequence which, when extended by one nucleotide, are indicative of the presence or absence of a polymorphism. Detection of the polymorphisms in the primer

extension reaction facilitated by the use of distinctively labeled ddNTPs in the primer extension reaction.

The methods of claims 1 and 36 (and their dependent claims) differ significantly from those disclosed by Anastasio et al. and/or Goelet et al. These claims require both the use of multiplex amplification primers and the use of a plurality of extension primers capable of detecting a plurality of CYP2D6 polymorphisms. Specifically, claims 1 and 36 require the multiplex use of the amplification primers of SEQ ID NOs: 1-4 and 5-8 respectively. None of the cited prior art discloses the multiplex use of these amplification primers. For this reason alone, claims 1 and 36 are novel over Anastasio et al. as evidence by Goelet et al. The remaining pending but rejected dependent claims incorporate all of the limitations of the independent claims and are, therefore, also novel. These rejections are traversed and should be withdrawn.

Rejections Under 35 U.S.C. §103

Claims 5 and 23

Claims 5 and 23 stand rejected as obvious over Anastasio et al. in light of the teachings of Goelet et al., in view of Dovichi et al. (Methods Mol. Biol. 167: 225-239, 2001). The Examiner applies Anastasio et al. in light of Goelet et al. as described above, and notes that neither reference teaches the use of capillary electrophoresis. The Examiner alleges that the teachings of Dovichi et al., when combined with those of Anastasio et al. and Goelet et al. render obvious the rejected claims. Applicants respectfully traverse this rejection.

Claim 1, from which claim 5 depends, is not *prima facie* obvious because the cited prior art does not teach every element of the rejected claims. As discussed above, claim 1 requires the multiplex use of the amplification primers of SEQ ID NOs: 1-4. Neither Anastasio et al. nor Goelet et al. teach or suggest the use of multiplex amplification of CYP2D6 gene sequences, in any form, prior to the claimed primer extension reaction. Dovichi et al. does not remedy this

deficiency (i.e., does not teach the claimed amplification primers), nor is it asserted by the Examiner for that purpose.

Claim 23 is canceled herewith, rendering the remainder of this rejection moot. Accordingly, this rejection is traversed and should be withdrawn.

Claims 10, 28, 36-37, 39, and 41-42

Claims 10, 28, 36-37, 39, and 41-42 stand rejected as obvious over Anastasio et al. in light of the teachings of Goelet et al., in view of Pastinen et al. (PCR Applications; Innis, M.A. et al., eds., Academic Press, San Diego, 1999, pp. 521-535). The Examiner applies the combination of Anastasio et al. and Goelet et al. as discussed above, and notes that Pastinen et al. discloses detecting the CYP2D6*4 allele by primer extension using a primer comprising SEQ ID NO: 9. Applicants respectfully traverse this rejection.

Independent claims 1 and 36 are not *prima facie* obvious because the cited prior art does not teach every claim element. Specifically, claims 1 and 36 require the multiplex use of the amplification primers of SEQ ID NOs: 1-4 and 5-8, respectively. Pastinen et al. does not teach or suggest performing multiplex amplification prior to the primer extension reaction, let alone a multiplex amplification using Applicants' claimed primers. Thus, Pastinen et al. does not remedy the deficiencies of the basic combination of Anastasio et al. and Goelet et al., as applied against claims 1 and 36, and their dependent claims.

Claim 19 is canceled herewith, rendering the remainder of this rejection moot. Accordingly, this rejection is traversed and should be withdrawn.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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